richard carchman

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Cc: "chris_coggins" <chris_coggins@direcway.com>; "Haussmann, Hans-Juergen" <HansJ.Haussmann@pmintl.com>

Sent: Sunday, June 06, 2004 10:42 AM

Subject: Re:

I agree. Changing a single risk factor by a few percent likely would have a small impact and possibly not detectable in a clinical study. However, if several risk factors are each reduced by only a small percent, the overall effect could be significant. Based on the Munster PROCAM study, the myocardial infarction (MI) risk model of Assmann et al. (2002) is a multiple function of risk factors. For example, if six risk factors are each reduced by only 4%, the overall estimated risk is $0.96^6 = 0.78x$ original risk (over a 20% risk reduction). This could probably be best demonstrated by measuring risk factors in current smokers and then measuring risk factors in the same smokers after switching to a potentially reduced risk product. The baseline values for each smoker serves as their own control, thereby eliminating many confounding factors. The risk for each smoker would be estimated before and after switching. The hypothesis of reduced _estimated_ risk of MI in the group of smokers in such a clinical trial could be tested by a paired statistical test. Easier said than done, but appears feasible and could be done in a relatively short period of time. Perhaps a later long-term study of MI incidence would be required for verification.
Dave Gaylor

----- Original Message -----
From: richard carchman
To: debbie ; david gaylor ; George_J_Patskan_1 ; Sanders, Edward ; Martin.Unverdorben unvr ; bakrissab
Cc: chris_coggins ; Haussmann, Hans-Juergen
Sent: Sunday, June 06, 2004 7:09 AM

I was wondering about rather than focusing on a change in any **one** potential biomarker of effect (eg LDL) why can't we take a more global view of a prep and look at what eg Framingham or the Chinese report that I commented on from the recent JAMA article. We could look at all of the currently 'accepted' biomarkers of effect and try to develop an indicator or pattern change for **each** subject, giving appropriate weight to these biomarkers. Since we don't know which smoke constituents and in which subjects there might be some change and the fact that when it comes to something like CVD, which has at least 300 risk factors, not all the subjects will be the same in terms of background and ongoing events(eg normalizing for age, sex, socioeconomic factors only gets you so far) what are the prospects for such an approach being of value? Any way this a an early Sunday morning thought. Richard

6/6/2004